VIA MEDICA

ORIGINAL ARTICLE

Cardiology Journal
2015, Vol. 22, No. 2, 160–164
DOI: 10.5603/CJ.a2014.0052

ISSN 1897–5593

Prognostic utility of ischemic response in functional imaging tests (SPECT or stress echocardiography) in low-risk unstable angina patients

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Abstract

Background: *The aim of this study is to determine the ability of ischemic response in imaging stress tests (single-photon emission computed tomography [SPECT] or stress echocardiography [SE]) to predict events in low-risk unstable angina patients.*

Methods: *Three hundred and fifty-nine patients with unstable angina (< 24 h), asymptomatic at admission, without ST-segment elevation or depression, normal troponins, and undergoing SPECT (n = 188) or SE (n = 171) during hospitalization (median = 1 day) were included. A positive imaging test (IMAGING+) was defined as the presence of reversible perfusion defects or wall motion abnormalities in at least 2 contiguous segments. Multivariate models were constructed using these results and clinical variables to predict events at 6 months.*

Results: *Ninety-nine (27%) patients had IMAGING+, 72/188 (38%) in SPECT and 27/17 (16%) in SE (p < 0.0001). Events occurred in 84 (23%) patients: 4 had myocardial infarction, 47 new hospitalizations due to angina and 33 coronary artery revascularizations. Independent predictors of coronary artery disease were: IMAGING+ (OR: 6.4, 95% CI: 3.4–11.8, p < 0.0001), history of coronary artery disease (OR: 2.5, 95% CI: 1.2–5.2, p < 0.02) and TIMI risk (OR: 1.5, 95% CI: 1.1–2.2, p < 0.03).*

Conclusions: *In low-risk unstable angina patients, an ischemic response in functional stress tests (SPECT or SE) was associated with adverse events and severe coronary artery disease.* (Cardiol J 2015; 22, 2: 160–164)

Key words: unstable angina, functional test, prognostic

Introduction

The management of acute coronary syndromes (ACS) is a common challenge for a cardiologist. Nowadays, an invasive strategy characterized by coronary angiography followed by revascularization is clearly recommended in high-risk patients presenting with ST-segment or non-ST segment elevation ACS [1].

Yet, little attention has been paid to the management of patients initially stratified as having low risk, who represent a relatively high percentage of hospitalizations due to chest pain. Despite these patients have a favorable short-term outcome,

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Received: 31.05.2014 Accepted: 13.06.2014

approximately 15% will suffer a new event within the first year, particularly new hospitalization and revascularization [2, 3].

Guidelines recommend hospitalized low-risk patients with negative troponins, absence of electrocardiographic abnormalities and who remain without symptoms to undergo an exercise stress test for further risk stratification. Imaging tests provide higher diagnostic yield, but are recommended in special cases [1, 4].

In our environment, imaging tests, particularly sestamibi cardiac scan (single-photon emission computed tomography — SPECT) or stress echocardiography (SE), are frequently used to evaluate patients with ACS once they become stable. The value of both tests in chronic patients is unquestionable; yet, their usefulness in patients with ACS, which constitutes a completely different scenario, has not been adequately explored [5–10].

The aim of the present study is to determine if the ischemic response in imaging tests is related with an unfavorable outcome in patients hospitalized with low-risk unstable angina without significant predictors of risk.

Methods

All the patients hospitalized due to definite or probable unstable angina between 2008 and 2010, and who underwent imaging tests during the hospitalization at Instituto Cardiovascular de Buenos Aires were considered for the study. Then, patients with the following criteria were selected: (1) Angina within 24 h before admission; (2) Absence of symptoms during hospitalization; (3) Absence of electrocardiographic abnormalities suggestive of acute ischemia; (4) Troponin T < 0.01 ng/mL; (5) Absence of significant valvular heart disease of cardiomyopathies.

A total of 359 patients with these criteria were enrolled during 2 years and were followed-up during 6 months. These patients were evaluated with SPECT (n = 188) or SE (n = 171) during hospitalization (median = 1 day) according to each patient's characteristics. Most patients (324; 90%) underwent exercise stress testing, and pharmacological stress testing was used in the rest. The information about the demographic characteristics, clinical data and outcomes were retrieved from the medical records. For each patient, a Thrombolysis in Myocardial Infarction (TIMI) risk score was assigned at admission [11].

Protocols of imaging stress tests

Imaging stress tests, either with exercise or with pharmacological stress, were performed within 48 h after admission (normally in the first 24 h). The type of stress was selected according to the availability of the test, the preference of the treating physician and the patient's ability to exercise.

SPECT: After an intravenous line was placed, the patient underwent an exercise stress test in bicycle ergometer or treadmill, or received intravenous dipyridamole, 40 mg (as pharmacological stress) followed by intravenous aminophylline. Tc 99m-labeled sestamibi was injected at peak stress, and images were acquired after eating a fatty meal. Rest images were acquired after a second infusion, during the same day. SPECT was considered positive (SPECT+) in the presence of reversible perfusion defects (improved defect at rest) in at least 2 contiguous segments.

SE: The test was performed following the recommendations of the American Society of Echocardiography [12], using a Philips Envisor HD ultrasound system with digital images and integrated acquisition protocols, using second harmonic imaging. Exercise was performed in a supine bicycle bed and images were acquired at rest, during exercise and after exercise. For pharmacological stress, dobutamine was administered by intravenous infusion at incremental doses plus atropine to achieve 85% of the theoretical maximum heart rate.

Stress echocardiography was considered positive (SE+) when new or worsening wall motion abnormalities developed in at least 2 contiguous segments.

Finally, positive imaging test (IMAGING+) was defined as SPECT+ or SE+.

Coronary angiography: Only 63 (18%) patients with inducible ischemia or new hospitalization due to angina and suspected coronary artery disease (CAD) underwent coronary angiography, as the guidelines consider that performing this method to low-risk patients without inducible ischemia or symptoms is not ethical. Severe CAD was defined as stenosis ≥ 70% measured by quantitative angiography in at least one coronary artery.

Follow-up: Only patients who had been followed up during 6 months by review of the electronic medical record or by telephone were included.

Statistical analysis

Continuous variables were expressed as mean and median, and analyzed using the t test or the Wil-

Table 1. Differences between patients with positive and negative tests.

Variable	IMAGING (+) N = 99 (28%)	IMAGING (–) N = 260 (73%)	P
Age	63 ± 10	56 ± 11	< 0.01
Female	14 (14%)	87 (33%)	< 0.05
Diabetes mellitus	23 (23%)	33 (13%)	< 0.05
Previous myocardial infarction	42 (42%)	48 (20%)	< 0.01
TIMI risk score	2.64 ± 1.04	1.78 ± 1.23	< 0.01
History of coronary artery disease	65 (65%)	65 (25%)	< 0.01

coxon signed-rank test according to the distribution. Discrete variables were expressed as percentages and analyzed by the χ^2 test. All the variables with a p value < 0.10 at the univariate analysis were included in the multivariate logistic regression analysis to detect severe coronary stenosis. Multivariate models were constructed, considering the total group (IMAGING). All the calculations were performed using the StatsDirect 1.7.3 software.

Results

Correlation between the clinical data, demographics and imaging tests

An ischemic response (IMAGING+) was seen in 99 (28%) patients: 38% with SPECT and 16% with SE (p < 0.01). The characteristics of the patients with positive and negative tests are compared in Table 1. Patients with ischemic tests were older, diabetics, men, had a history of infarction or CAD and a higher TIMI risk score.

Correlation between the results of imaging tests and invasive coronary angiography.

Sixty-three (18%) patients underwent coronary angiography, 50/99 with ischemic response (50%) and 13/260 (5%) without ischemic response (p < 0.01). Severe CAD was detected in 56/63 (89%) patients. Patients with ischemic response presented more evidence of documented CAD than the rest (44/99 and 12/269, p < 0.001). Severe CAD was present in 27/31 (87%) patients with ischemic response by SPECT and in 17/19 (89%) patients with ischemic response by SE (p = NS).

Table 2 shows the independent predictors of severe CAD after multivariate logistic analysis. An image test with ischemic response was the main independent predictor, increasing the risk of having severe CAD by 13 times, which was above historical variables as history of CAD and TIMI risk score.

Table 2. Significant predictors of severe coronary artery disease (CAD) at multivariate analysis (p < 0.03).

Variable	Odds ratio	95% CI
Ischemic response	13.1	5.9–30.0
History of CAD	3.7	1.6–8.7
TIMI risk score > 2	2.7	1.1–6.4

CI — confidence interval

Clinical follow-up and cardiovascular events

Events were detected in 23% of the 359 patients, and included 4 acute myocardial infarctions, 47 new hospitalizations due to angina and 33 coronary artery revascularizations (27 percutaneous coronary interventions and 6 coronary artery bypass graft surgeries). The results of the tests and the events are shown in Table 3.

Outcome predictors

The ischemic response in the imaging test was the most important independent predictor, increasing the risk of events by 6.4 times. The other significant clinical variables were history of CAD and TIMI risk score, increasing the risk by 2.5 and 1.5 times, respectively. Even after excluding revascularization, an imaging test with ischemic response was a predictor of events. Table 4 shows significant independent predictors identified by logistic regression.

Discussion

The management of patients with ACS has become standardized. Most recommendations agree in the necessity of interventional therapy in high-risk patients. In the same sense, low-risk patients should not be intervened as they have better outcomes and revascularization does not offer greater advantages in these patients. How-

Table 3. Ischemic response and events at 6 months.

Variable	Total (n = 359)	SPECT group (n = 188)	SE group (n = 171)	P
Ischemic response	99 (27%)	72 (38%)	27 (16%)	< 0.0001
New hospitalization	42 (12%)	25 (13%)	17 (10%)	NS
Acute myocardial infarction	4 (1%)	4 (2%)	0 (0%)	NS
Revascularization	38 (11%)	27 (14%)	11 (5%)	< 0.03
Total events	84 (23%)	54 (29%)	30 (18%)	< 0.02
Events excluding revascularization	46 (13%)	27 (14%)	19 (11%)	NS

Table 4. Significant predictors of events in multivariate analysis.

Variable	Total events OR (95% CI)	P
IMAGING (+) (n = 359)	6.4 (3.4–11.8)	< 0.01
History of coronary artery disease	2.5 (1.2–5.2)	< 0.002
TIMI risk score	1.5 (1.1–2.2)	< 0.03
SPECT positive (n = 188)	3.9 (1.7–8.5)	< 0.02
Stress echocardiography positive (n = 171)	9.2 (2.52–33.8)	< 0.001

OR — odds ratio; CI — confidence interval

ever, among the patients discharged from hospital with diagnosis of low-risk unstable angina, 1 or 2 out of 10 will require new hospitalization for new symptoms, unusually due to myocardial infarction, or will require new revascularization (either by percutaneous intervention or surgery) within 6 months after discharge.

Detecting the patients who will develop events among the low-risk group has always been complicated. However, a high percentage of events occur in these patients, who are very frequent in clinical practice. These patients should be differentiated from those evaluated in the emergency room with doubtful presentations, constituting a group with lower risk requiring hospitalization in a very small percentage of cases.

There are few publications of low-risk unstable angina patients undergoing any imaging stress test, including conventional exercise stress test, SPECT or SE [13–17]. Despite the prognostic significance of these tests is different in acute patients, the results are interpreted using the risk criteria for stable angina.

In our environment, SPECT is frequently used for risk stratification and prognostic evaluation. The decision to use SPECT or SE depends, in most cases (as it happened in this study) on the availability of each test, trying to avoid hospital delays.

The results of our study suggest that the presence of an ischemic response in imaging stress tests predicts the development of events in the short-term. One of 4 patients will exhibit an ischemic response (defined as transient perfusion defects or wall motion abnormalities) and in these patients the risk of events is 6 times higher and statistically significant, with a narrow confidence interval.

This diagnostic yield of imaging stress tests in the group classified by the guidelines as low-risk unstable angina patients is greater than the one of the other predictors analyzed in this sample: history of CAD and TIMI risk score widely used in the coronary care units for prognostic stratification.

The decision between using SPECT or SE was not the aim of this study, and the question of which test is better cannot be answered with the information obtained. Both tests were independent predictors of events, including revascularization.

New hospitalizations and revascularization are considered soft cardiac events, and revascularization cannot be independent of the result of the functional test. However, hard cardiac events, as mortality or myocardial infarction, are difficult to detect in a low-risk population [18]. In addition, keeping the result of the test secret would have been the only way to make revascularization independent of the result of the tests, but this can only be achieved with a prospective and blind design.

For this reason, we also analyzed the predictive value of the tests to detect CAD in diagnostic coronary angiography. Also in this case the ischemic response was a predictor of severe coronary artery stenosis. Yet, the percentage of coronary

angiographies was low and conditioned by the results of the stress tests.

Conclusions

In low-risk unstable angina patients, an ischemic response in functional stress tests (SPECT or SE) is more precise than clinical parameters as history of CAD and TIMI risk score to predict events at 6 months, particularly new hospitalization, revascularization and severe coronary artery stenosis. These tests seem to be useful to guide a medical or an invasive strategy in this group of patients.

Conflict of interest: None declared

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